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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/448,378

11/23/1999

KENNETH BRASEL

2836-D

4973

22932

7590

04/12/2005

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/448,378

Applicant(s)

BRASEL ET AL.

Examiner

Phillip Gambel

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6, 7, 20, 22-26, 30-35 and 37-56 is/are pending in the application.
- 4a) Of the above claim(s) 54-56 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6, 7, 20, 22-26, 30-35, 37-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 1/12/05, has been entered.

Applicant's amendment, filed 1/12/05, has been entered.

Claims 27, 29, 36 have been canceled. Claims 1-5, 8-19, 21, have been canceled previously.

Claims 7, 25, 26, 34 and 35 have been amended

Claims 6, 7, 20, 22-26, 28, 30-35 and 37-56 are pending.

Applicant's election without traverse of Group I and the species GM-CSF has been acknowledged.

Claims 54-56 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Action will be in response to applicant's amendment, filed 1/12/05.

The rejections of record can be found in the previous Office Actions.

3. As indicated previously, the filing date of the instant claims is deemed to be the filing date of the priority application USSN 08/539,142, i.e. 10/4/95.

4. Upon reconsideration of applicant's amended claims, filed 1/12/05, the previous rejection under 35 U.S.C. § 112, first paragraph, written description, has been withdrawn.

5. Applicant's arguments, filed 1/12/05, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant in conjunction with a Statement by Applicant's representative concerning a claim of common ownership between the present application and Lyman et al. (WO 94/28391) have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that because the primary reference has been disqualified, the rejection under 35 USC § 103(a) / § 102(e) may be properly removed.

Applicant has provided evidence in this file showing that the invention was owned by, or subject to an obligation of assignment to, the same entity as Lyman et al. (WO 94/28391) at the time this invention was made, or was subject to a joint research agreement at the time this invention was made. However, Lyman et al. (WO 94/28391) qualifies as prior art under another subsection of 35 U.S.C. § 102 (that is, 35 U.S.C. § 102(a)), and therefore, is not disqualified as prior art under 35 U.S.C. § 103(c).

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Applicant may overcome the applied art either by a showing under 37 CFR 1.132 that the invention disclosed therein was derived from the invention of this application, and is therefore, not the invention "by another," or by antedating the applied art under 37 CFR 1.131.

As pointed out previously, PCT International Application WO 94/28391, which stems from the patent family that spawned the previous prior art of record Lyman et al. (U.S. Patent No. 5,943,423), is less than a year from the present application earliest effective filing date of 10/4/95 and is by another and, in turn, does qualify as prior art.

35 USC § 102(c) is drawn to subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of Section 102 and not based upon 35 USC § 102(a). See MPEP 706.02(I).

Claims stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lyman et al. (WO 94/94/28391; 1449) in view of Elliott et al. (U.S. Patent No. 5,478,556), Srivastava et al. (U.S. Patent No. 6,017,544) and Brem et al. (U.S. Patent No. 5,626,862) essentially for the reasons set forth in the previous Office Actions.

The following is reiterated for applicant's convenience.

The instant claims are drawn to methods of augmenting immune responses in cancer patients with FLT3-ligand and GM-CSF.

Lyman et al. teach methods of treating cancer patients by administering FLT3-L in combination with other cytokines, including GM-CSF including treating intestinal damage resulting from irradiation and chemotherapy and stimulating immune responses as well as hemopoietic cells to improve the quality of life of a patient (see entire document; Background of the Invention; Summary of the Invention, including Claims). Lyman et al. teach the FLT3-L and its recombinant forms and sequences encompassed by the claimed invention (See Detailed Description of the Invention and Examples).

Lyman et al. differs from the claimed methods by not disclosing the known administration of a tumor antigen to a cancer patient to induce an immune response to the desired tumor antigen and that the administration of FLT3-L and/or GM-CSF would lead to an increase in the number of dendritic cells per se.

Both Elliott et al. and Srivastava teach that GM-CSF teach the known administration of GM-CSF with tumor antigens to simulate the immune system.

Elliott et al. teach the vaccination of cancer patients with tumor associated antigens mixed with cytokines, including GM-CSF, including the stimulation of antigen-processing (see entire document, Background of the Invention, Summary of the Invention, Detailed Description of the Invention). Both the tumor associated antigens and the GM-CSF can be administered at various times (see Summary of the Invention).

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Srivastava teach methods of augmenting cancer vaccines with cytokines including GM-CSF (see entire document, including Summary of the Invention, including column 4, paragraph 6; Detailed Description, including column 12, paragraph 3; Claims.). Srivastava teach compositions comprising cancer cells as well as cancer antigens serve as sources for immunization against tumor antigens of interest (See entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention). In addition to combining cancer therapies, including surgery, radiation therapy and chemotherapy (columns 5-6, overlapping paragraph), dosages and modes of administration depend on variables known and practiced in the art at the time the invention was made (e.g. see columns 11-12, Formulation and Administration of the Complexes). Srivastava teach that a number of tumor types, including fibrosarcoma, can be treated (see column 6, paragraphs 4-5).

Brem et al. teach that GM-CSF is a cytokine that systematically activates cytotoxic T lymphocytes which have shown to lead to the elimination of tumor cells in a potent and specific manner, by stimulating the growth and activity of several myeloid cells and playing a critical role in the migration and development of professional antigen presenting cells such as dendritic cells (see column 8, paragraph 2).

Given the teachings of combining FLT3-L and GM-CSF to treat cancer by Lyman et al. in combination with the teachings of Elliott et al. and Srivastava et al. that GM-CSF was potent in cancer vaccination, one of ordinary skill in the art would have combined FLT3-L, GM-CSF and tumor antigens to stimulate the hemopoietic and immune system of cancer patients, including the vaccination to tumor associated antigens. Given the teachings of stimulating the hemopoietic and immune systems with FLT3-L and GM-CSF with the teachings of administering tumor antigens to activate immune responses and antigen presentation, one of ordinary skill in the art would have had an expectation of success that the administration of FLT3-L and GM-CSF would increase the number of dendritic cells, as evidenced by the teachings of Brem et al. that GM-CSF activates immune responses via dendritic cells.

Given the teachings of the prior art to treat and augment immune responses in cancer patients and that the administration of cytokines and tumor antigens were based on variables and procedures known and practiced by the ordinary artisan, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer tumor antigen at various times with respect to cytokine administration, including the administration of tumor antigen prior, concurrently and after cytokine administration.

One of ordinary skill in the art at the time the invention was made would have been motivated to select a combination of cytokines, including FLT3-L and GM-CSF in combination with tumor antigens to treat human cancer; given the properties of said cytokines to augment immune responses including augmenting immune responses to cancer antigens and to stimulate hemopoietic cells to alleviate the effects of chemotherapy and radiation therapy in cancer patients.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

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6. No claim is allowed.

7. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, PhD.
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April 11, 2005